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Abstract The goal of this article is to provide an useful criterion of positivity and well-posedness for a wide range of infinite dimensional semilinear abstract Cauchy problems. This criterion is based on some weak assumptions on the non-linear part of the semilinear problem and on the existence of a strongly continuous semigroup generated by the differential operator. To illustrate a large variety of applications, we exhibit the feasibility of this criterion through three examples in mathematical biology: epidemiology, predator-prey interactions and oncology.

Keywords Positivity · Well-Posedness · Dynamic Systems · Semilinear Problems · Population Dynamics

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1 Introduction

In a wide range of mathematical modelling of natural phenomena, the quantities that are described through the mathematical system have to satisfy some

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positivity properties to ensure physical reality. For instance, when considering the evolution of matter quantities, such as in biology (or also physics [1], chemistry [2],...), the positivity of the solutions of the underlying dynamical system is a crucial prerequisite to achieve the well-posedness of the problem and to guarantee its physical relevance.

A significant proportion of dynamical systems that describe the evolution over time of matter quantities are non-linear, but it oftenly appears that the non-linear effects can be seen as perturbations of linear dynamics, leading to such a differential formulation:

$$\begin{cases} y'(t) = \overbrace{Ay(t)}^{\text{linear dynamics}} + \overbrace{f(y(t),t)}^{\text{perturbations}}, t \geq 0, \\ y(0) = y_0, \end{cases} \tag{1}$$

where $y(t)$ denotes the modeled matter quantity at time t, that mathematically lies in a Banach Lattice. When imposing a non-negative initial condition y_0, the question of positivity is then crucial to study. In the case of a finite dimensional operator A, this question has been extensively studied (see [3] and references therein for general results). However, to our knowledge, we don't know any general criterion of positivity in the case where A is a differential operator, *i.e.* when the first equality in (1) rewrites as partial differential equations (PDEs), while such differential operators are extensively used in mathematical biology, or also in many other applied mathematical sciences. For instance, in the specific case of biology, let us mention the use of structured population dynamics models, where the operator is of transport type, or the use of diffusive processes, where models incorporate a Laplacian operator (see [4] for a review of positivity results in reaction-diffusion systems).

The goal of this article is to provide an useful criterion of well-posedness and positivity for the semilinear problem (1) for wide ranges of linear differential operators A and non-linear functions f, and then to illustrate the feasibility of this criterion through three examples of models arising from mathematical biology: epidemiology, predation and oncology.

This article is structured as follows: Section 2 is dedicated to the introduction of three concrete biological models, described by semilinear PDEs, for which the positivity of solutions must necessarilly be satisfied. Then we tackle in Section 3 the formulation and the proof of the criterion of positivity and well-posedness. This criterion is based on the formulation of an abstract semilinear Cauchy Problem, studied using a semigroup approach. Finally, in Section 4, we apply the criterion to the biological models of Section 2 to prove the well-posedness and the positivity of their solution.

2 Three biological examples

In this section, we introduce three examples of semilinear evolutionary problems in mathematical biology for which the positivity and well-posedness have

to be proved for biological purpose. The matter quantities that are modelled in those three examples, *i.e.* populations, predator/prey or cell densities, evolve with respect to the time $t \geq 0$. The epidemiological and predator-prey models deal with transport process, with a non-constant velocity in the epidemiological case and a non-local boundary condition in the predator-prey case, while the model in oncology deals with diffusive PDEs.
One can note that through those specific examples, a large spectrum of biological models are involved: PDE structured population models (see [5] and references therein) and reaction-diffusion models.

Epidemiology The first example on which we focus deals with epidemiology. When modeling the transmission of disease between individuals, a common way is to split the population densities into two sub-classes that are the susceptible class (S) and the infected class (I). From such a splitting results the classical epidemiological model of SI type [6]. Furthermore, lots of diseases (influenza, HIV, prion pathologies...) have a varying intensity during their evolution that may be important to take into account in the modeling process. This phenomena was recently described in [7,8], where the disease intensity was incorporated into the infected class, leading to the formulation of the following infection load-structured epidemiological model of transport type:

$$\begin{cases} S'(t) = \gamma - (\mu_0 + \alpha)S(t) - S(t)\mathcal{T}(\beta I)(t),\ t \geq 0, \\ \partial_t I(t,i) = -\partial_i(\nu i I(t,i)) - \mu(i)I(t,i) + \phi(i)S(t)\mathcal{T}(\beta I)(t),\ t \geq 0,\ i \in J, \\ \nu i^- I(t,i^-) = \alpha S(t),\ t \geq 0, \\ S(0) = S_0, \quad I(0,\cdot) = I_0(\cdot), \end{cases} \tag{2}$$

where the infection load is $i \in J = (i^-, +\infty) \subset \mathbb{R}_+$, $\mathcal{T}$ is the integral operator defined for some integrable fonction h on J by

$$\mathcal{T} : h \to \int_J h(i)di$$

and the epidemiological parameters satisfy the following assumptions:

- $\beta,\ \mu_0,\ \nu,\ \alpha > 0$ and $\gamma \geq 0$;
- $\phi \in \mathcal{C}^\infty(J)$ is a non-negative function such that $\lim_{i \to +\infty} \phi(i) = 0$ and $\int_J \phi(i)di = 1$, $\mu \in L^\infty(J)$ is such that $\mu(i) \geq \mu_0$ for almost every $i \in J$.

For a biological relevance, it is clear that for each positive initial condition $(S_0, I_0(\cdot))$, the densities $S(t)$ and $I(t,\cdot)$ in Problem (2) have to remain positive whenever they exist.

Predator-prey interactions When considering predator-prey interactions, the age of the prey is a key factor of selection for the predator. It is therefore natural to add a structuration of the prey densities according to their age. In doing so, the classical Lotka-Volterra model, that was initially an ODE model [9], turns into the following PDE model, that is developed in [10]:

$$\begin{cases} \partial_t x(t,a) + \partial_a x(t,a) = -\mu(a)x(t,a) - y(t)\gamma(a)x(t,a), \ t \geq 0, \ a \geq 0, \\ y'(t) = \alpha y(t) \int_0^\infty \gamma(a)x(t,a)da - \delta y(t), \ t \geq 0, \ a \geq 0, \\ x(t,0) = \int_0^\infty \beta(a)x(t,a)da, \ t \geq 0 \\ x(0,\cdot) = x_0(\cdot), \ y(0) = y_0, \end{cases} \tag{3}$$

where x and y denote the density of preys and predators, respectively. The assumptions on the parameters are the following:

- $\alpha \in]0,1[$, $\delta > 0$ are constant parameters that respectively denote the assimilation coefficient of ingested preys and the basic mortality rate of the predators;
- $\mu, \gamma, \beta \in L^\infty_+(\mathbb{R}_+)$ are age-dependent functions that represent, respectively, the basic mortality rate of the preys, the predation rate and the birth rate.

To ensure a certain realism, we want that the densities of preys x and predators y remain positive given a positive initial data (x_0, y_0).

Oncology The third application is a model that describes the growth of a brain tumour published in [11]. The model aims at studying a treatment method of tumor cells through a problem of controllability. The tumor and normal cells are in competition for the resources and are subject to a drug treatment whose role is to decrease the cell densities. Even if some normal cells are destroyed, the key point here is that the drug affects more the tumor ones.
To make explicit the model, let us consider Ω a bounded domain of $\mathbb{R}^N$, $N \in \mathbb{N}^*$, with boundary $\partial\Omega$ of class $\mathcal{C}^2$ and for a fixed $T > 0$, let $Q_T = \Omega \times (0,T)$ and $\Sigma_T = \partial\Omega \times (0,T)$. The evolution problem is then written using the following three semilinear heat equations, where the variables (t,x) are delibarately avoided for a better reading:

$$\begin{cases} \partial_t y_1 = d_1 \Delta y_1 + a_1 g_1(y_1) y_1 - (\alpha_{1,2} y_2 + \kappa_{1,3} y_3) y_1, \\ \partial_t y_2 = d_2 \Delta y_2 + a_2 g_2(y_2) y_2 - (\alpha_{2,1} y_1 + \kappa_{2,3} y_3) y_2, \\ \partial_t y_3 = d_3 \Delta y_3 - a_3 y_3 + u, \\ \partial_n y_i(t) = \nabla y_i(t) \cdot \mathbf{n} = 0, \ t \geq 0, i \in \{1, ..., 3\}, \\ y(x,0) = y_0(x), \ x \in \Omega, \end{cases} \tag{4}$$

where $\mathbf{n}$ denotes the external normalized normal to the boundary $\partial\Omega$. Here $y_1(t,x)$ stands for the density of tumor cells, $y_2(t,x)$ the density of normal tissue and $y_3(t,x)$ the drug concentration at any vector position x and time t. In the latter problem, the growth rates of cells are defined by the functions g_i according to the following logistic shape:

$$g_i(y_i) = 1 - y_i/k_i.$$

The assumptions on the parameters are the following:

- $d_i > 0$ are the coefficients for the space diffusive effect;
- $a_i > 0$, where a_1, resp. a_2, denotes the tumor cell intrinsic growth rate, resp. the normal tissue intrinsic growth rate and a_3 is the drug reabsorption coefficient;
- $k_i > 0$ denote the carraying capacity of the medium;
- $\alpha_{i,j} > 0$ are coefficients that translate the interspecific competition between tumor and normal cells;
- $\kappa_{1,3} \gg \kappa_{2,3} > 0$ are the degradation rates due to the treatment;
- $u(x,t) \geq 0$ represents the flux of injected drug over time at position x.

Similarly to the previous biological examples, we aim at proving well-posedness and positivity of the solution.

3 A criterion of positivity and well-posedness

In all this section, let us consider $(\mathcal{W}, +, \|\cdot\|_{\mathcal{W}}, \geq)$ a Banach Lattice (see [12, p. 6]), *i.e.* an partially ordered Banach space for which any given elements x, y of $\mathcal{W}$ have a supremum $\sup(x,y)$ and for all $y_1,\ y_2,\ y_3 \in \mathcal{W}$ and $\alpha \geq 0$,

$$\begin{cases} y_1 \leq y_2 \Rightarrow (y_1 + y_3 \leq y_2 + y_3 \text{ and } \alpha y_1 \leq \alpha y_2), \\ |y_1|_{\mathcal{W}} \leq |y_2|_{\mathcal{W}} \Rightarrow \|y_1\|_{\mathcal{W}} \leq \|y_2\|_{\mathcal{W}}, \end{cases} \tag{5}$$

with, for all $y \in \mathcal{W}$, $|y|_{\mathcal{W}} = \sup(y, -y)$. We will denote by $\mathcal{W}^+ = \{y \in \mathcal{W} : 0 \leq y\}$ the non-negative cone and for every $m > 0$ by B_m the ball of $\mathcal{W}$ of radius m.

We consider in this work the system

$$\begin{cases} y'(t) = Ay(t) + f(y(t), t),\ \ t \geq 0 \text{ in } \mathcal{W}, \\ y(0) = y_0 \qquad\qquad\qquad\qquad\quad\ \text{in } \mathcal{W}, \end{cases} \tag{6}$$

where $A : D(A) \subset \mathcal{W} \to \mathcal{W}$ is an infinitesimal generator of a $\mathcal{C}_0$ semigroup $(T_A(t))_{t\geq 0}$, $y'(t)$ is an element of $\mathcal{W}$ and $f : \mathcal{W} \times \mathbb{R}^+ \to \mathcal{W}$ is continuous in t and locally Lipschitz continuous in y uniformly in t in the following sense: for every $m > 0$ there exists a constant $k_m > 0$ such that for every $z_1, z_2 \in B_m$,

$$\|f(z_1,t) - f(z_2,t)\|_{\mathcal{W}} \leq k_m \|z_1 - z_2\|_{\mathcal{W}},\ \forall t \in \mathbb{R}^+.$$

Finally, let us briefly remind that for a fixed $T \in]0,\infty]$, a *mild solution* of Problem (6) on $[0,T[$ is a function $y \in \mathcal{C}([0,T[;\mathcal{W})$ that satifies the integral equation

$$y(t) = T_A(t)y_0 + \int_0^t T_A(t-s) f(y(s),s)\mathrm{d}s.$$

Remark 1 Since $\mathcal{W}^+$ is closed (see [12]), we deduce that for all $T > 0$, the order $\geq$ is compatible with the integration in time, more precisely, for all $x, y \in \mathcal{C}([0,T];\mathcal{W})$,

$$(x(t) \geq y(t)\ \forall\ t \in [0,T]) \Rightarrow \int_0^T x(s)\mathrm{d}s \geq \int_0^T y(s)\mathrm{d}s. \tag{7}$$

The following theorem, that states well-posedness and positivity property for the solution of Problem (6), is the main result of the present article:

Theorem 1 *Let $y_0 \in \mathcal{W}^+$. We suppose that*

(i) A is generator of a positive $\mathcal{C}_0$ semigroup on $\mathcal{W}$, i.e. $T_A(t)\mathcal{W}^+ \subset \mathcal{W}^+$ for all $t \geq 0$,
(ii) for all $m > 0$, there exists $\lambda_m \in \mathbb{R}$ such that, for all $z \in \mathcal{C}(\mathbb{R}^+; \mathcal{W}^+ \cap B(0,m))$,

$$f(z(t),t) + \lambda_m z(t) \geq 0, \quad \forall t \geq 0. \tag{8}$$

Then there exists $t_{max} \in]0,\infty]$ such that system (6) has an unique positive mild solution $y \in \mathcal{C}([0,t_{max}[;\mathcal{W})$. Moreover, if $t_{max} < \infty$,

$$\lim_{t \to t_{max}} \|y(t)\|_{\mathcal{W}} = \infty.$$

The main idea of the proof is to perform a vectorial translation to the range values of the non-linear part f so that they remain in $\mathcal{W}^+$. This translation is then compensated by the substraction of a linear term to the differential operator, that does not affect its spectral and positivity properties. Consequently, we shall study the following system in the proof of the theorem:

$$\begin{cases} y'(t) = (A - \lambda I)y(t) + f(y(t),t) + \lambda y(t), \ t > 0 & \text{in } \mathcal{W}, \\ y(0) = y_0 & \text{in } \mathcal{W}. \end{cases} \tag{9}$$

Lemma 1 *Let A be an infinitesimal generator of a positive $\mathcal{C}_0$ semigroup. Then, for every $\lambda \in \mathbb{R}$, $A - \lambda I$ is an infinitesimal generator of a positive $\mathcal{C}_0$ semigroup.*

Proof As a bounded perturbation of A, $A - \lambda I$ is an infinitesimal generator of a $\mathcal{C}_0$ semigroup $(T_{A-\lambda I}(t))_{t\geq 0}$ on $\mathcal{W}$ (see [13, p. 76]). A $\mathcal{C}_0$ semigroup on a Banach Lattice is positive if and only if the resolvent $(\mu I - L)^{-1}$ of its generator L is positive for all sufficiently large μ (see [14, p. 207]). Thus there exists μ^* such that, for all $x \in \mathcal{W}$ and all $\mu > \mu^*$, $(\mu I - A)^{-1}x \geq 0$. Consequently, for all $x \in \mathcal{W}$ and all $\mu > \mu^* - \lambda$, we have $(\mu I - A + \lambda I)^{-1}x \geq 0$. Then $A - \lambda I$ is an infinitesimal generator of a positive $\mathcal{C}_0$ semigroup.

Proof (Proof of Theorem 1.1) Since A is generator of a positive $\mathcal{C}_0$ semigroup $(T_A(t))_{t\geq 0}$, there exists $\omega, M \geq 1$ such that, for all $t \in \mathbb{R}^+$,

$$\|T_A(t)\|_{\mathcal{W}} \leq Me^{\omega t}.$$

Lemma 1 then implies that for evey $\lambda \in \mathbb{R}$, $A - \lambda I$ is also generator of a positive $\mathcal{C}_0$ semigroup $(T_{A-\lambda I}(t))_{t\geq 0}$. Moreover, it is easy to check that for all $t \in \mathbb{R}^+$,

$$\|T_{A-\lambda I}(t)\|_{\mathcal{W}} \leq Me^{\omega t}, \quad \forall \lambda \in \mathbb{R}. \tag{10}$$

Let $t_0 \in (0,1)$, $m = 2M\, e^{\omega}\|y_0\|_{\mathcal{W}}$ and λ_m that satisfies (8). Consider the set $\Gamma_m = \{y \in \mathcal{C}([0,t_0];\mathcal{W}) : y(0) = y_0, y(t) \geq 0, \|y(t)\|_{\mathcal{W}} \leq m, \forall t \in [0,t_0]\}$.

The continuity properties of the lattice operations (see [12]) imply that Γ_m is a non-empty closed subset of $\mathcal{C}([0,t_0];\mathcal{W})$.

Consider now the mapping ψ, defined on Γ_m by

$$\psi(y)(t) = T_{A-\lambda_m I}(t)y_0 + \int_0^t T_{A-\lambda I}(t-s)\left[f(y(s),s)+\lambda_m y(s)\right]\mathrm{d}s, \quad t\in[0,t_0].$$

We aim at proving that ψ has a unique fixed point in Γ_m.
Let us start by proving that ψ preserves Γ_m. The positivity of $(T_{A-\lambda_m I}(t))_{t\geq 0}$ and the positivity assumption (8) clearly imply that $\psi(y)\in\mathcal{C}([0,t_0];\mathcal{W}^+)$. Furthermore, from the inequality (10), one deduces that

$$\begin{aligned}\|\psi(y)(t)\|_{\mathcal{W}} \leq Me^{\omega t}\|y_0\|_{\mathcal{W}} + Me^{\omega t}\int_0^{t_0} &(\|f(y(s),s)-f(0,s)\|_{\mathcal{W}}\\ &+\|f(0,s)\|_{\mathcal{W}}+\lambda_m\|y(s)\|_{\mathcal{W}})\mathrm{d}s.\end{aligned}$$

The time continuity property on f induces the existence of $\gamma>0$ (independent of $t_0<1$) such that for every $y\in\Gamma_m$ and every $t\in(0,t_0)$,

$$\|\psi(y)(t)\|_{\mathcal{W}} \leq Me^{\omega}(\|y_0\|_{\mathcal{W}} + t_0(mk_m+\gamma+m\lambda_m)).$$

Thus, for $t_0=\min\{1,\|y_0\|_{\mathcal{W}}\times(mk_m+\gamma+m\lambda_m)^{-1}\}$ we have $\|\psi(y)(t)\|_{\mathcal{W}}\leq 2Me^{\omega}\|y_0\|_{\mathcal{W}}=m$ and so $\psi(y)\in\Gamma_m$.
We now prove that ψ is contractant in the following sense: for every $y,z\in\Gamma_m$, every $n\in\mathbb{N}^*$ and every $t\in[0,t_0]$,

$$\|\psi^n(y)(t)-\psi^n(z)(t)\|_{\mathcal{W}} \leq \frac{[Me^{\omega}t(k_m+\lambda_m)]^n}{n!}\sup_{t\in[0,t_0]}\|y(t)-z(t)\|_{\mathcal{W}}. \quad (11)$$

Let us prove (11) by induction. Clearly the Lipschitz assumption on f implies that

$$\|\psi(y)(t)-\psi(z)(t)\|_{\mathcal{W}} \leq Me^{\omega}\,(k_m+\lambda_m)\,t\sup_{\theta\in[0,t_0]}\|y(\theta)-z(\theta)\|_{\mathcal{W}},$$

and equality (11) holds for $n=1$. Suppose now that (11) holds for a $k\in\mathbb{N}^*$. Then for all $t\in[0,t_0]$,

$$\begin{aligned}&\|\psi^{k+1}(y)(t)-\psi^{k+1}(z)(t)\|_{\mathcal{W}}\\ &\leq (Me^{\omega}(k_m+\lambda_m))\int_0^t\|\psi^k(y)(s)-\psi^k(z)(s)\|_{\mathcal{W}}\mathrm{d}s,\\ &\leq \frac{[Me^{\omega}(k_m+\lambda_m)]^{k+1}}{k!}\sup_{\theta\in[0,t_0]}\|y(\theta)-z(\theta)\|_{\mathcal{W}}\int_0^t s^k\mathrm{d}s,\end{aligned}$$

and (11) is true for $k+1$ and consequently for every $n\in\mathbb{N}^*$ by induction. Finally, we can apply the Banach's fixed point theorem to conclude that ψ has a unique fixed point $\bar{y}$ in Γ_m. Systems (6) and (9) being equivalent, $\bar{y}$ is a mild solution of (6). Then some standard time extending properties of the solution induce that the solution $\bar{y}$ is defined on a maximal interval $[0,t_{max}[$. To finish, we prove the uniqueness of the solution on the whole space $\mathcal{C}([0,t_{max}(\bar{y})[,\mathcal{W}^+)$. If $\bar{z}$ is another mild solution defined on $[0,t_1[$ with $t_1 < t_{max}(\bar{y})$, then, denoting $R = \max_{\theta\in[0,t_1]}\{\|\bar{y}(\theta)\|_{\mathcal{W}}, \|\bar{z}(\theta)\|_{\mathcal{W}}\}$, we obtain for all $t \in [0,t_1]$,

$$\|\bar{y}(t)-\bar{z}(t)\|_{\mathcal{W}} \leq Me^{\omega t_1}k_R\int_0^t \|\bar{y}(s)-\bar{z}(s)\|_{\mathcal{W}}\mathrm{d}s.$$

Then $\|\bar{y}(t)-\bar{z}(t)\|_{\mathcal{W}} = 0$ by a standard Gronwall argument and $\bar{y} = \bar{z}$ in $[0,t_1]\times\mathcal{W}$. Furthermore, if $t_{max}(\bar{y}) < \infty$, since $\|\bar{z}(t)\|_{\mathcal{W}} = \|\bar{y}(t)\|_{\mathcal{W}}$ for all $t < \min\{t_{max}(\bar{y}), t_{max}(\bar{z})\}$ and $\lim_{t\to t_{max}(\bar{y})}\|\bar{y}(t)\|_{\mathcal{W}} = \infty$, we deduce that the maximal intervals of existence of $\bar{y}$ and $\bar{z}$ are equal.

4 Illustrations of the criterion in mathematical biology

In this section, we exhibit the application of well-posedness and positivity criterion on the three biological examples of Section 2.

Epidemiology Consider the Banach Lattice $X = \mathbb{R}\times L^1(J)$, X^+ the non-negative cone of X and $y_0 = (S_0, I_0) \in X^+$. Then it is clear that Problem (2) can rewrite as (6), where the function $f : X \to X$ and the differential operator $A : D(A) \subset X \to X$ are given by

$$f(u,v) = \begin{pmatrix} f_1(u,v) \\ f_2(u,v)\end{pmatrix} = \begin{pmatrix}\gamma - u\mathcal{T}(\beta v)\\ \phi u\mathcal{T}(\beta v)\end{pmatrix},\ A = \begin{pmatrix} -\mu_0-\alpha & 0 \\ 0 & -\frac{d}{di}(\nu i\cdot)-\mu\end{pmatrix},$$

with $D(A) = \{(x,\varphi)\in X, (i\varphi)\in W_1^1(J) \text{ and } \varphi(i^-) = \alpha x\}$. In [7], the authors prove that the differential operator $(A, D(A))$ is an infinitesimal generator of a positive $\mathcal{C}_0$ semigroup $(T_A(t))_{t\geq 0}$ on X and that function f is locally Lipschitz continuous on X. Moreover, for every $m > 0$ and every $(\bar{S},\bar{I}) \in \mathcal{C}(\mathbb{R}^+; X^+\cap B(0,m))$, one gets, denoting $\lambda_m = m\beta$,

$$\begin{cases} f_1(\bar{S}(t),\bar{I}(t)) + \lambda_m\bar{S}(t) \geq \gamma + \bar{S}(t)(\lambda_m - \beta\mathcal{T}(\bar{I}(t))) \geq 0,\\ f_2(\bar{S}(t),\bar{I}(t)) + \lambda_m\bar{I}(t) = \phi\bar{S}(t)\mathcal{T}(\beta\bar{I}(t)) + \lambda_m\bar{I}(t) \geq 0.\end{cases}$$

Thus, condition (8) of Theorem 1 is satisfied and there exists $t_{max} \in]0,\infty]$ such that Problem (2) has an unique mild solution (S,I) in $\mathcal{C}([0,t_{max}[,X^+)$.

Predator-prey interactions Let $X = L^2(\mathbb{R}^+)\times\mathbb{R}$, X^+ the non-negative cone and $(x_0,y_0)\in X^+$. Considering the operator $A : D(A)\subset X\to X$ and the functional $f : X \to X$ given by

$$f(\phi,z) = \begin{pmatrix} f_1(\phi,z)\\ f_2(\phi,z)\end{pmatrix} = \begin{pmatrix} -\alpha z\gamma\phi \\ \widetilde{\alpha}\int_0^\infty \gamma(a)\phi(a)da\end{pmatrix},\ A = \begin{pmatrix} L & 0\\ 0 & -\delta\end{pmatrix},$$

with $D(A) = \{(\phi,z)\in X, (\phi,z)\in W_1^1(\mathbb{R}^+) \text{ and } \varphi(0) = \int_0^\infty \beta(a)\phi(a)da\}$ and $L\phi = -\phi' - \mu\phi$. The map f is clearly locally Lipschitz continuous on X.

Furthermore, under the assumption that there exists $\mu_0 > 0$ such that $\mu(a) \geq \mu_0$ f.a.e. $a \in \mathbb{R}$, it is proved in [10] that the operator A is the infinitesimal generator of a positive $\mathcal{C}_0$ semigroup $(T_A(t))_{t\geq 0}$ on X. Then, for all $m > 0$, denoting $\lambda_m = \alpha m\gamma$, we obtain for every $(\bar{x}, \bar{y}) \in \mathcal{C}(\mathbb{R}^+; X^+ \cap B(0, m))$

$$\begin{cases} f_1(\bar{x}(t), \bar{y}(t)) + \lambda_m \bar{x}(t) \geq \bar{x}(t)(\lambda_m - \alpha m\gamma) \geq 0, \\ f_2(\bar{x}(t), \bar{y}(t)) + \lambda_m \bar{y}(t) \geq 0. \end{cases}$$

Again, condition (8) of Theorem 1 holds and the existence of $t_{max} \in]0, \infty]$ such that system (3) has an unique mild solution (x, y) in $\mathcal{C}([0, t_{max}[, X^+)$ is ensured.

Oncology Let $X = L^2(\Omega; \mathbb{R}^3)$, X^+ the corresponding non-negative cone, $y_0 \in X^+$ and $u \in L^2(Q_T)^+$. Then system (4) can be reformulated as (6) where

$$\begin{cases} f(y) = (g + h)(y) + (0, 0, u)^*, \\ g(y) = \mathrm{diag}(a_1 g_1(y_1) y_1, a_2 g_2(y_2) y_2, a_3 g_3(y_3) y_3), \\ h(y) = \mathrm{diag}(-(\alpha_{1,2} y_2 + \kappa_{1,3} y_3) y_1, -(\alpha_{2,1} y_1 + \kappa_{2,3} y_3) y_2, 0), \\ A = \mathrm{diag}(d_1 \Delta, d_2 \Delta, d_3 \Delta). \end{cases}$$

The existence of the semigroup $(T_A(t))_{t\geq 0}$ is a consequence of the Lumer-Phillips Theorem (see [13, p. 14]) for maximal dissipative operators. Indeed, in the present case, A is clearly maximal dissipative since it is defined with Laplacian operators. Using the maximum principle of the heat equation, the semigroup is positive.

Consequently, when taking $\lambda_m = \max\{m(a_1/k_1 - \alpha_{1,2} - \kappa_{1,3}), m(a_2/k_2 - \alpha_{2,1} - \kappa_{2,3}), a_3\}$ for $m > 0$, we obtain the following estimations for all $\bar{y} = (\bar{y}_1, \bar{y}_2, \bar{y}_3) \in \mathcal{C}(\mathbb{R}^+; X^+ \cap B(0, m))$

$$\begin{cases} f_1(\bar{y}) + \lambda_m \bar{y}_1 = a_1 g_1(\bar{y}_1)\bar{y}_1 - (\alpha_{1,2}\bar{y}_2 + \kappa_{1,3}\bar{y}_3)\bar{y}_1 + \lambda_m \bar{y}_1 \\ \qquad\qquad\qquad \geq \bar{y}_1[\lambda_m - m(a_1/k_1 - \alpha_{1,2} - \kappa_{1,3})] \geq 0, \\ f_2(\bar{y}) + \lambda_m \bar{y}_2 = a_2 g_2(\bar{y}_2)\bar{y}_2 - (\alpha_{2,1}\bar{y}_1 + \kappa_{2,3}\bar{y}_3)\bar{y}_2 + \lambda_m \bar{y}_2 \\ \qquad\qquad\qquad \geq \bar{y}_2[\lambda_m - m(a_2/k_2 - \alpha_{2,1} - \kappa_{2,3})] \geq 0, \\ f_3(\bar{y}) + \lambda_m \bar{y}_3 = -a_3 \bar{y}_3 + u + \lambda_m \bar{y}_3 \geq \bar{y}_3(\lambda_m - a_3) \geq 0. \end{cases}$$

Thus condition (8) is satisfied and, using Theorem 1, there exists $t_{max} \in]0, \infty]$ such that problem (4) has an unique mild solution (x, y) in $\mathcal{C}([0, t_{max}[, X^+)$.

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